

A6
cont.

36. (New) An isolated oligonucleotide having at least about 30 contiguous nucleotides of SEQ ID NO:3, encompassing an allele at amino acid 44, wherein amino acid 44 is isoleucine, and further encompassing an allele at amino acid 51, wherein amino acid 51 is alanine.

37. (New) The isolated oligonucleotide of claim 36, wherein nucleotides 130-132 ATA, and nucleotides 151-153 are GCC.

38. (New) The isolated oligonucleotide of claim 36, wherein nucleotides 130-132 are ATC, and nucleotides 151-153 are GCC

REMARKS

Claims 1-7 and 10-17 stand rejected under one or more of 35 U.S.C. § 101, § 112, first and second paragraphs, and § 102(e). Claims 1, 11, and 15 have been amended as indicated above, and claims 2 through 7, 10, 12, 13, 14, and 16 have been cancelled from the application. New claims 32 through 38 have been added to the application. Support for these claims is found in the specification, for example, at page 8, lines 14 through 17, and at page 29, lines 20 through 25. The specification has also been amended to correct an obvious typographical error at page 30, line 28. Support for this amendment is found elsewhere in the specification, for example at page 29, line 12. Applicants affirm their election to prosecute claims directed to the invention of Group I as set forth by the Examiner (claims 1-7 and 10-17, i.e., SEQ ID NO:3)

Objections

The examiner objected to the specification for containing an embedded hyperlink on page 50, line 25. The specification has been amended to remove this embedded hyperlink and others that Applicants have noted. In the format as amended, the addresses are believed to be sufficient to allow those of ordinary skill in the art to navigate to the respective web sites, but they will not appear as active embedded hyperlinks in electronic forms of the specification. Accordingly, Applicants request that the objection to the specification be withdrawn.

The Examiner objected to claim 1 as reciting non-elected SEQ ID NO:1 and SEQ ID NO:14. Claim 1 has been amended to remove reference to these sequences; accordingly, Applicants request that the objection be withdrawn.

Rejections Under 35 U.S.C. §§ 101, and 112, First Paragraph

Claims 1-7 and 10-17 have been rejected under 35 U.S.C. § 101 as the invention allegedly is not supported by either a specific and substantial asserted utility or a well-established utility. According to the Examiner, the claims are directed to isolated nucleic acids encoding proteins, and while Applicants defined the proteins as belonging to the human Interleukin-1 family, the specification allegedly does not disclose any information regarding the functional characteristics or biological activity of the protein. The Examiner goes on to assert that functional information can be automatically derived from structural information only to a limited extent. The claims have also been rejected under 35 U.S.C. § 112, first paragraph, on the grounds that when a claimed invention lacks utility, one skilled in the art would not know how to use the invention. Applicants respectfully disagree with both rejections for the reasons set forth below.

Applicants have amended the claims to more particularly point out and distinctly claim what they regard as their invention. As amended, the claims are directed to specific nucleic acids based on the structure (sequence) of those nucleic acids, and do not recite polypeptides or proteins. Thus, while disagreeing with the Examiner's statement that Applicants have not taught a specific utility for polypeptides encoded by the presently claimed nucleic acids, Applicants respectfully assert that the utility or lack thereof of a polypeptide or polypeptides is not pertinent to the present claims. Rather, the utility of the claimed invention must be based on the utility of the nucleic acids themselves.

On page 30 of the specification, beginning at line 22, Applicants disclose that the DNA of SEQ ID NO:1 (which is a fragment of the longer DNA of SEQ ID NO:3) maps to human chromosome 2, region 2q11-12. Several disease states also map to human chromosome 2, including glaucoma, ectodermal dysplasia, insulin-dependent diabetes mellitus, wrinkly skin syndrome, T-cell leukemia/lymphoma, and tibial muscular dystrophy. Thus, as stated in the specification, those of skill in the art can use the claimed nucleic acids to analyze abnormalities associated with genes mapping to chromosome 2.

Furthermore, as disclosed in Example 1, and discussed at page 8, lines 5 through 18, Applicants identified polymorphisms associated with this particular member of the IL-1 family, at amino acids 44 and 51. Oligonucleotides that encompass any of the alleles associated with these amino acids (encoded by nucleotides 130-132 and nucleotides 151-153, respectively) are useful for detecting polymorphisms associated with disease. Such oligonucleotides include the full-length DNA of SEQ ID NO:3, as well as oligonucleotides derived therefrom, claims to which have been added in this amendment.

Applicants respectfully assert that these utilities are specific, that is they are applicable to the claimed subject matter, not to the broad class of the invention (i.e., these

utilities are not shared by every nucleic acid or oligonucleotide). As stated in *the Manual of Patent Examining Procedure*, Edition 8 (August 2001), at 2107.01, "a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target." (emphasis denoted by underlining added) Such is not the case here, where a specific DNA target is disclosed.

Moreover, the aforementioned utilities are substantial: they define a real world context of use, as shown in the attached Exhibits (Exhibit 1: Dale and Nicklin, *Genomics* 57:177-179, 1999, demonstrating that investigators find use in nucleic acids that facilitate mapping of the region of chromosome 2 to which several members of the IL-1 family have been mapped; Exhibit 2: U.S. Patent 6,268,142, demonstrating that diagnostics for polymorphisms in IL-1 family members are useful and desirable). Use of the claimed nucleic acids to analyze abnormalities associated with genes mapping to chromosome 2 and use of the claimed nucleic acids and/or oligonucleotides for detecting polymorphisms associated with disease are reasonable uses that provide a clear public benefit.

The Exhibits also demonstrate that the asserted utilities are credible; they are neither inconsistent with known scientific principles, nor speculative. Accordingly, the claimed invention is supported by at least one specific and substantial (and well-known) utility; Applicants request that the rejection under 35 U.S.C. § 101 be withdrawn. Moreover, inasmuch as the claimed invention possesses utility, one of ordinary skill in the art would know how to make and use it in light of the disclosure, as discussed above; Applicants request that the rejection under 35 U.S.C. § 112 also be withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 7 and 10 have been rejected under 35 U.S.C. § 112, second paragraph, as reciting a fragment of a DNA wherein the fragment has IL-1 activity. Claims 7 and 10 have been cancelled, without regard to the instant rejection. Applicants specifically do not acquiesce in the Examiner's assertion that the metes and bounds of the claim could not be ascertained. However, in light of the cancellation, the rejection is moot, and Applicants request that it be withdrawn.

Rejections under 35 U.S.C. § 102

Claims 1-7 and 10-17 have been rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,339,141. The claims have been amended to refer to nucleic acids having the sequence shown in SEQ ID NO:3, which differs from that shown in U.S. Patent No. 6,339,141. Accordingly, this reference does not anticipate the invention as

claimed, and the examiner is therefore requested to withdraw the rejection of the claims under 35 U.S.C. § 102(e).

CONCLUSIONS

Claims 1, 11, 15, 17 and 32 through 38 are currently under consideration in the application and stand rejected under 35 U.S.C. §§ 101, 112, first and second paragraphs, and 102(e). It is believed that these grounds for rejection have been overcome by virtue of the amendments and comments set forth above. Newly added claims 32 through 38 are believed to be allowable for the same reasons. Accordingly, the applicants believe that the claims are in condition for allowance and notification to that effect is respectfully requested. If further issues remain in this application, the examiner is asked to contact the undersigned at her direct dial number given below.

Respectfully submitted,



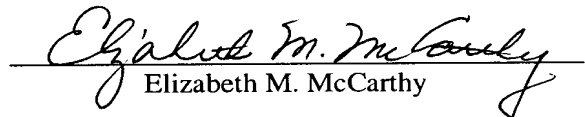
Patricia Anne Perkins
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DIRECT DIAL: 206-265-4782

Correspondence address:

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents, Washington, D.C. 20231, on the date indicated below.

Date: February 24, 2003


Elizabeth M. McCarthy

Appendix to Amendment A

(marked up version of specification and claims amended by the attached Amendment)

In the Specification:

A number of screening techniques that include the use of cell based or in vitro based specific binding assays or tests are known. (See, for example, *High Throughput Screening: The Discovery of Bioactive Substances*, John P. Devlin (ed.), Marcel Dekker, New York, 1997, ISBN: 0-8247-0067-8., <http://www.lab-robotics.org/>, ~~<http://www.sbsonline.org/>~~, and the web sites for the Laboratory Robotics Interest Group ("lab-robotics.org/") and the Society for Biomolecular Screening ("sbsonline.org/") all of which are incorporated herein by reference) When combined with integrated robotic systems, high throughput screening techniques can be used to test and screen large collections of chemical compounds and/or natural products for antagonist or agonist activity within a short amount of time. Specific assays or tests include homogeneous assay formats such as fluorescence resonance energy transfer, time resolved fluorescence resonance energy transfer, fluorescence polarization, scintillation proximity assays, reporter gene assays, fluorescence quenched enzyme substrate, chromogenic enzyme substrate and electrochemiluminescence, as well as, more traditional heterogeneous assay formats such as enzyme linked immunosorbant assays (ELISA) or radioimmunoassays. Homogeneous assays are mix and read style assays that are very amenable to robotic application, whereas heterogeneous assays require separation of bound analyte from free analyte by more complex unit operations such as filtration, centrifugation or washing. These assays can be utilized to detect a wide variety of specific biomolecular interactions and the inhibition of specific biomolecular interactions by small organic molecules, drug candidates, antibodies, peptides and other antagonists and/or agonists. Specific biomolecular interactions include, but are not limited to, protein-protein interactions, receptor-ligand interactions, enzyme-substrate interactions, etc.

(paragraph spanning pages 50 and 51)

For example, chromosomes can be mapped by radiation hybridization. PCR is performed using the Whitehead Institute/MIT Center for Genome Research Genebridge4 panel of 93 radiation hybrids
(~~http://www.genome.wi.mit.edu/ftp/distribution/human_STS_releases/july97/rhmap/genebridge4.html~~
at the Whitehead Institute/MIT web site "genome.wi.mit.edu/ftp/distribution/human_STS_releases/july97/rhmap/genebridge4.html"). Primers are used which lie within a putative exon of the gene of interest and which amplify a product from human genomic DNA, but do not amplify hamster genomic DNA. The results of the PCRs are converted into a data vector that is submitted to the Whitehead/MIT Radiation Mapping site on the internet (~~<http://www.seq.wi.mit.edu>~~ "seq.wi.mit.edu"). The data is scored and the chromosomal assignment and placement relative to known Sequence Tag Site (STS) markers on the radiation hybrid map is provided. The following web site provides additional information about radiation hybrid mapping:

"genome.wi.mit.edu/ftp/distribution/human_STS_releases/july97/07-97.INTRO.html"

http://www-genome.wi.mit.edu/ftp/distribution/human_STS_releases/july97/07-97.INTRO.html).

(page 30, at lines 9-21)

As set forth below, the DNA of SEQ ID NO:1, has been mapped by high-throughput-shotgun sequencing to the 2q11-12 region of human chromosome 2. Human chromosome 2 is associated with specific diseases which include but are not limited to glaucoma, ectodermal dysplasia, insulin-dependent diabetes mellitus, wrinkly skin syndrome, T-cell leukemia/lymphoma, and tibial muscular dystrophy. Thus, the nucleic acids of SEQ ID NO:1, SEQ ID NO:3, or a fragment thereof can be used by one skilled in the art using well-known techniques to analyze abnormalities associated with genes mapping to chromosomes 2. This enables one to distinguish conditions in which this marker is rearranged or deleted. In addition, nucleic acid fragments of SEQ ID NO:1 or a fragment thereof can be used as a positional marker to map other genes of unknown location.

(page 30, at lines 22 through 31)

In the Claims:

1. (amended) An isolated DNA selected from the group consisting of:
 - (e) DNA comprising SEQ ID NO:4 3;
 - (f) DNA comprising SEQ ID NO: 3, with the proviso that nucleotides 130-132 are selected from the group consisting of ACA, ATA and ATC;
 - (g) DNA comprising SEQ ID NO:3, with the proviso that nucleotides 151-153 are selected from the group consisting of GAC and GCC; and
 - (h) DNA comprising SEQ ID NO:3 with the proviso that nucleotides 130-132 are selected from the group consisting of ACA, ATA and ATC and nucleotides 151-153 are selected from the group consisting of GAC and GCC;
 - ~~(i) DNA comprising nucleotides 29-487 SEQ ID NO:14~~
 - ~~(j) DNA that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2;~~
 - ~~(k) DNA that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:4;~~
 - ~~(l) DNA that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:4, with the proviso that the amino acid at residue 44 is selected from the group consisting of threonine and isoleucine and the amino acid at residue 51 is selected from the group consisting of aspartic acid and alanine.~~
 - ~~(m) DNA that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:15;~~
 - ~~(n) DNA comprising a DNA that is degenerate from the DNA of (a) through (i)~~
 - ~~(o) DNA comprising a DNA that is at least 80% identical to the DNA of (a) (j); and,~~

~~(p) DNA comprising a DNA that encodes amino acids 1 through 152 of SEQ ID NO:4.~~

11. (Amended) A vector comprising the DNA of claim ~~3~~ 1.
15. (Amended) A host cell comprising a vector of claim ~~14~~ 11.